Editorial Views

The Reticular Activating System Revisited

It is now two decades since French, Verzeano, and Magoun proposed that anesthetics might act by reversibly blocking neural conduction within the reticular activating system (RAS), thereby diminishing "arousal" subserved by this area.\(^1,2\) In this issue, Cucchiara and Michenfelder have contributed further to understanding pathologic cerebral function and the role of the RAS in anesthesia. Their investigation focused on two significant questions: 1) Is there a relationship between decreased RAS activity and the anesthetic state? 2) Is decreased cerebral functional activity produced by transection of the RAS accompanied by decreased metabolic activity? These questions were approached by the simple expedient of measuring cerebral oxygen utilization (CMRO\(_2\)) before and after administration of thiopental to normal dogs and to animals whose RAS had been surgically destroyed. Their data suggest that RAS denervation is accompanied by functional but not metabolic depression. The decreases in CMRO\(_2\) following thiopental administration were similar in the two groups of animals. The authors concluded that neither RAS denervation nor decreased CMRO\(_2\) is uniquely causative of the anesthetic state and that functional and metabolic activities in the central nervous system need not change in parallel fashion.

That a change in RAS function is not the sole cause of anesthesia has been suggested by a number of recent studies. Clark et al. evaluated somatosensory evoked potentials in man receiving subanesthetic concentrations of cyclopropane.\(^4\) They were able to record both directly transmitted impulses and nonspecific or extralemniscal traffic. The latter represented function of the RAS. Administration of less than 4.3 per cent cyclopropane abolished both specific and nonspecific transmission of experimental stimuli. At a time when both evoked potentials were abolished (remember that classic theory would hold that obliteration of nonspecific transmission through the RAS would diminish arousal), the subjects responded to command and could react to sensory input. Clearly, consciousness was maintained when RAS function was depressed. As expected, anesthetic concentrations of cyclopropane also obliterated both specific and nonspecific transmission.\(^5\) The ability to depress RAS function selectively did not appear to be a valid explanation of cyclopropane's anesthetic action. Furthermore, studies of different agents disclosed that each affected neural function in a different manner.\(^6,7\) Nitrous oxide abolished nonspecific activity, as did low concentrations of diethyl ether. Concentrations of ether greater than 4 per cent obliterated the entire somatosensory evoked potential. Enflurane produced a specific evoked response of abnormally long latency and high amplitude. Darbinjan et al. postulated that diethyl ether did not interfere with RAS function, but depressed synaptic input into this area of the central nervous system.\(^8\) The work of Cucchiara and Michenfelder adds further evidence against the simplistic proposal that all anesthetics exert their effects by selective depression of RAS activity.

What is the significance of the apparent lack of correlation between normal CMRO\(_2\) and depressed cerebral function which followed
transsection of the RAS? A likely explanation is that the authors measured total rather than regional oxygen uptake. Ingvar and Risberg measured regional cerebral blood flow of man at “mental rest” and while the subjects did mental arithmetic.9 The latter task resulted in measurable increases in cerebral blood flow (and presumably CMRO2) in discrete areas of the brain. Similar studies disclosed an increase in occipital lobe metabolic activity accompanying photic stimulation. It is interesting that Cucchiara and Michenfelder found that restriction of sensory input from the eyes had no apparent effect on overall CMRO2. Cerebral trauma or marked cerebral edema with increased intracranial pressure is usually accompanied by both unconsciousness and decreased CMRO2. This is not unexpected, since large portions of the brain are involved by these processes. On the other hand, the profound functional effects produced by RAS transection may have been mediated by abnormal activity of only a few small areas within the brain. In such a case, the regional metabolic depression would not be detected by measurement of total cerebral blood flow.

Finally, what of the effects of thiopental? Unlike RAS denervation, administration of this drug affects activity of cells throughout the central nervous system. If failure to detect decreased oxygen utilization following RAS denervation resulted from the methodology employed, the concept that cellular metabolism and function are related may still be tenable. In such a case it would not be unexpected that CMRO2 should be diminished equally in normal and in denervated dogs following administration of the barbiturate, as Cucchiara and Michenfelder found.

Whether this depression of CMRO2 is either necessary or responsible for the anesthetic state is the moot point. Decreased CMRO2 is not produced by all anesthetics. Injection of ketamine may be accompanied by either increased 10 or unchanged 11 CMRO2. It is probably naive to say that anesthesia results from decreased cerebral oxygen consumption. One can only postulate that both the anesthetic state and decreased CMRO2 are secondary to some other primary process.

Cucchiara and Michenfelder have presented provocative and interesting work in an attempt to answer some significant questions. Their conclusions are reasonable based on the data they have developed. However, a complete picture is not yet available, and will not be forthcoming until studies of regional cerebral metabolism have been performed.

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References